

## IN THE SPECIFICATION

Please replace the paragraph that appears on page 42, lines 2 to 6, with the following paragraph:

In addition to dCTP daminase, *P. furiousus* P45 exhibits a significant, but lower degree of sequence similarity to uridine triphosphatase (dUTPase). dUTPase, an enzyme encoded by the *dut* gene, converts dUTP to pyrophosphate and dUMP. An amino acid sequence alignment comparing the sequence of P45 to several dUTPases is shown below. Regions of identity and regions of similarity are shown in black boxes, while ~~regions of similarity~~ are shown in grey boxes.

Please replace the sequence listing that appears after the abstract at page 76 with the enclosed sequence listing.

Please replace page 41 with the replacement page 41 enclosed herewith.

Please replace page 43 with the replacement page 43 enclosed herewith.



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### Example 9

#### Identification of Proteins Related to P45

##### 1. DNA Sequence Homology of *P. furiosus* P45 Protein to dCTP Deaminase and dUTPases

When the P45 DNA sequence was compared to multiple databases using the program BlastX, the probable deoxycytidine triphosphate deaminase (dCTP deaminase) gene (*dcd*) of *Desulfurolobus ambivalens* was found to exhibit the highest degree of similarity. The biochemical properties and physiological role of dCTP deaminase has been studied in *E. coli*, where dCTP deaminase is a homotetramer, which catalyzes the formation of dUTP and NH<sub>3</sub> from dCTP. DNA sequences with similarity to the *E. coli* *dcd* gene have been discovered in other bacteria (*Salmonella typhimurium*, *Haemophilus influenzae*) and in archaea (Ouzounis, C., Kyrpides, N., and Sander, C. Nucl. Acids Res. 23:565-570 (1995); Bult, C.J. et al. Science 273:1058-1073 (1996); Beck, C.J., Eisenhardt, A.R. and Neuhard, J., J. Biol. Chem. 250:609-616 (1975); Fleischmann, R.D. et al., Science 269:496-512(1995)). Amino acid sequence comparisons between *P. furiosus* P45 and the dCTP deaminases from *Desulfurolobus ambivalens* ("A") (also known as *Acidianus ambivalens*, *Sulfolobus ambivalens*), *E. coli* ("E"), and *Haemophilus influenza* are shown below, demonstrating sequence similarity ranges from about 39.1 to about 71.2%.

#### MAP Multiple Sequence Alignment Results

##### Page 1.1

1 P45	1	15 16	30 31	45 46	60 61	75 76	90	
2 A.	MLLPDWKIRKHE---	-ILIEPFSE-BWLOP AGYDLERVGXX XRVGR -----RAXVKKG-----LIDVKEK-----EGKVKXIPPREYAL						65
3 E.	MILCDRDLYKYLEKG WIVISPLTQ-DTIRS NGVDLRLVCG--EIAAR FKTDBIYEDGKDPR SFYBIEK-----GDEFPIIYPNEHVL							77
4 HAEIN	MRLCDTDIERYLDDG RLSINPRPPVERING ATIVDVRIGNPKRTFR GHTAAFIIDLSPGPDB VSAALDRVMSDBIVL DEGEAFLHLPGELAL							90

##### Page 2.1

1 P45	91	105 106	120 121	135 136	150 151	165 166	180	
2 A.	ILTLERIKLPDDVMG DMKIRSSSLAREGVIG SPAW--VDPGWDGNL TLMLYNASNEPVELR YGERPVQIAFIRLEG PARNPYR-----GNYQ							149
3 E.	LVTBEEVVKLPNDVMA FVNLRSRSPARLGLPV PPPI--VDAFPFGQL TIEVLG-SAPPVKIK RGTRPLHLLIPARTLT PVENPYH---GKYQ							160
4 HAEIN	ATTLESVILPADLVG WLDRGRSSSLARLGLMV HVTAAHRIDPGWSGCI VLRFYNSGKLPLALR PGMLIGALSFBPLSG PAVRPYINRREDAKYR							180

##### Page 3.1

1 P45	181	195 196	210 211	225 226	240 241	255 256	270	
2 A.	GSTRLLAPSKRKKL--	162	SEQ ID NO: 91					
3 E.	GOOGVTLPKPKFR--	173	SEQ ID NO: 91					
4 HAEIN	NOQGAVASRIDKD--	193	SEQ ID NO: 92					
		195	SEQ ID NO: 93					

*E. coli* DCD exhibits an apparent molecular weight of 21.2kD (Wang, L. and Weiss, B. J. Bacteriol. 174:5647-5653 (1992)), while the predicted molecular weight of *M. jannaschii* DCD is approximately 22kD (204 amino acids). These molecular weights are approximately half the apparent molecular weight of *P. furiosus* P45 and suggest that the heat-dissociated form of P45

